

Educational Case: Benign Papilloma of the Breast

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The following fictional case is intended as a learning tool within the Pathology Competencies for Medical Education (PCME), a set of national standards for teaching pathology. These are divided into three basic competencies: Disease Mechanisms and Processes, Organ System Pathology, and Diagnostic Medicine and Therapeutic Pathology. For additional information, and a full list of learning objectives for all three competencies, see <http://journals.sagepub.com/doi/10.1177/2374289517715040>.

Keywords

pathology competencies, disease mechanisms, organ system pathology, basement membrane, benign, breast, neoplasia, papilloma

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Primary Objective

Objective N2.1: Prevalence and Geographic Impact on Neoplasia. Describe the prevalence of neoplastic diseases and discuss the environmental factors that influence patients as they move between geographical regions.

Competency 1: Disease Mechanisms and Processes; Topic N: Neoplasia; Learning Goal 2: Environmental Influences on Neoplasia.

Secondary Objectives

Objective N2.2: Mechanisms of DNA Damage Repair. Describe the mechanisms by which exposure to radiation, tobacco, alcohol, or other environmental chemical agents can produce cancer.

Competency 1: Disease Mechanisms and Processes; Topic N: Neoplasia; Learning Goal 2: Environmental Influences on Neoplasia.

Objectives N3.1 through N3.5. Learning Goal 3: Characteristics of Neoplasia. Apply knowledge of the characteristics of neoplasia to discuss the morphologic appearance, classification, biological behavior, and staging of neoplasms.

Competency 1: Disease Mechanisms and Processes; Topic N: Neoplasia.

Objective BR1.1: Clinical Presentation of Breast Lesions. Identify the most frequently diagnosed breast lesions by age of the patient, based on the most common clinical presentations in males versus females.

Competency 2: Organ System Pathology; Topic BR: Breast; Learning Goal 1: Nonneoplastic Disorders of the Breast.

Objective BR1.4: Fibrocystic Change. Discuss the clinical significance of proliferative and nonproliferative fibrocystic change, with and without atypia, and describe how each of these changes and the family history affects the subsequent risk of developing breast cancer.

Competency 2: Organ System Pathology; Topic BR: Breast; Learning Goal 1: Nonneoplastic Disorders of the Breast.

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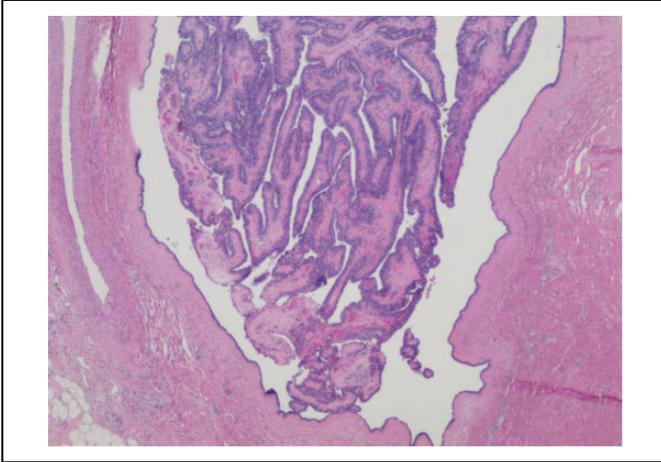


Figure 1. Low-power H&E image from core biopsy of breast.

Patient Presentation

A 37-year-old woman presents to her physician with a palpable density in her left breast. She noticed it 1 month ago and it hasn't changed in size. Her medical history is unremarkable. Medications include oral contraceptives. On examination, she appears somewhat anxious. Her vital signs are within normal limits. Physical examination is remarkable for an ill-defined area of firmness in the left breast in the upper outer quadrant adjacent to the nipple. The region is not tender, and there is no inflammation or discharge. A breast ultrasound core biopsy is obtained.

Questions/Discussion Points, Part I

Before jumping to the histologic sections, it is worth discussing the differential diagnosis based on the patient presentation.

What is the differential diagnosis of a palpable breast mass?

Our thinking is guided by the history. Is there pain? If so, is it within the breast or associated with the chest wall? Does it change with the hormonal cycle? Is there nipple discharge, and if so, what is its character? These distinctions help determine the likelihood of a true neoplasm of breast origin versus other physiologic possibilities. A thorough discussion is available in the study by Santen. Most importantly, 90% of new nodules presenting in premenopausal women are benign. In younger women, these are usually fibroadenomas, while “in the later reproductive period, hyperplasia, cysts, and carcinoma in situ are more common”.¹ As occurs elsewhere in the body, growths may also originate in nonglandular tissues including lipoma, fat necrosis (with a history of injury), and hemangioma. Imaging might suggest an area of increased density within the breast, not explained as simple cyst.

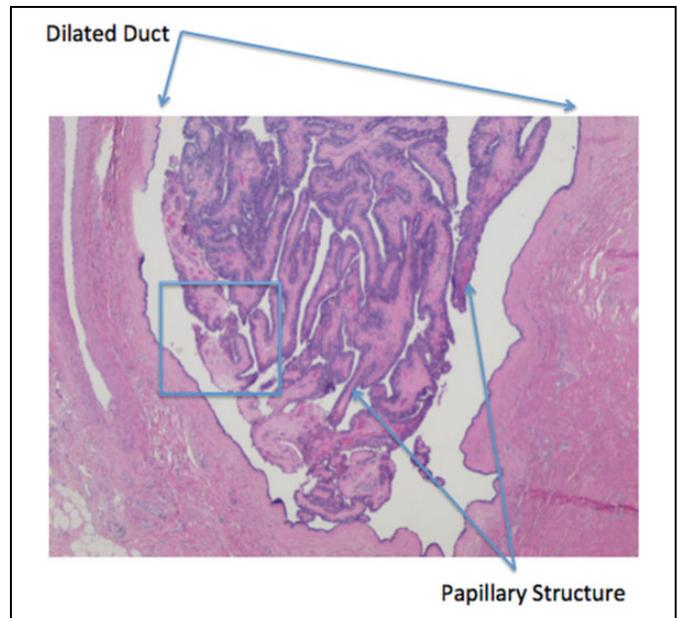


Figure 2. The image of Figure 1 is labeled showing the central papillary structure. A box encloses the region magnified below.

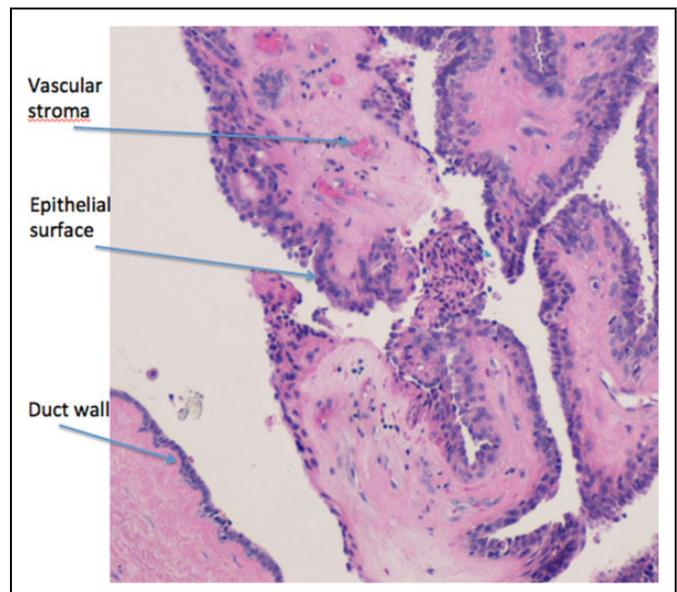


Figure 3. The comparison of the epithelial surface of the central fronds shows a monolayer of basophilic cells similar in appearance to the ductal lining and a fibrovascular eosinophilic stroma.

The biopsy was obtained (Figure 1). Describe the histologic features of this lesion. What is your diagnosis and what is its biologic behavior?

The low-powered Hematoxylin and Eosin (H&E)-stained slide obtained from the biopsy contains the field in Figure 1. Within a large dilated duct sits a structure folded into papillary fronds lined by a basophilic epithelium surrounding

a pink central fibrovascular stroma. These features are labeled in Figure 2.

A box in Figure 2 is seen at higher magnification in Figure 3. Figure 3 shows the duct wall and the epithelial surface of the papillary fronds to be composed of similar cells, forming a simple layer resting upon a basement membrane. The latter is not easy to see directly with these dyes but can be visually enhanced with special stains. Both tissues have matured in the manner characteristic for ductal tissue, with a polarized surface facing the duct lumen. The fronds also contain a stroma and small blood vessels. The structure is named an “intraductal papilloma.”

What Does the Name Tell You?

This is a benign proliferation in some ways analogous to adenomas that may occur elsewhere. If it had been malignant, the name would have included the word “carcinoma.” Papillomas have 2 main clinical presentations including solitary lesions near the nipple or multiple peripheral papillomas. The latter have a higher rate of atypia or malignancy arising in them. The most important observation is that there is no evidence of invasion. In other words, the epithelium does not penetrate the basement membrane and spread into adjacent areas. This proliferative neoplastic process can be associated with an increased risk of cancer in the future, especially if there is atypical piling up of the epithelial cells on each other (not seen here). In the absence of invasion, this lesion is benign and does not need further treatment. However, the patient should remain alert for changes in the future.

An additional important feature worth remembering is that neoplasia (new growth) includes benign lesions. These may grow to large size and can even become life threatening if they interfere with a function (eg, benign meningioma). Benign doesn’t mean, “you can live with it.” It means “not invasive.”

Other Manifestations of Benign Breast Disorders

Most important, benign lesions of the breast are much more common than malignancies. The incidence of these disorders changes with the age of the patient. An online review of Benign Breast Disease in Women is referenced.¹

Benign lesions of the breast are often classified in terms of their potential contribution to future breast cancer. In this light, there are 3 common categories:

- Nonproliferative changes (with little to no increased risk of cancer). This includes fibrocystic change and cysts;
- Proliferative lesions without atypia, including this case;
- Proliferative lesions with atypia.

Proliferative disease is associated with a 1.5- to 2-fold increased risk, while proliferative disease with atypia confers a 4- to 5-fold increased risk.²

What is the structure and function of the basement membrane that separates the epithelium from the fibrovascular core?

It is widely recognized that all epithelia organize themselves on a structure called the basement membrane. However, the relationship of the cell to this structure is much more interesting and active than many appreciate. Studies reveal “common functions that include the induction and maintenance of cell polarity, the establishment of barriers between tissue compartments, the organization of cells into tissues, and the protection of adherent cells from detachment-induced cell death, anoikis.”³ Although the term membrane is used, it is not a lipid membrane as the term is used elsewhere. Rather, the basement membrane is a complex type of extracellular matrix with an elaborate organization that includes collagen IV, laminins, other connective proteins and heparin sulfate containing proteoglycans. The absolute identity of the components of the basement membrane varies among cell types and are essential for the growth and maintenance of all epithelia.

Teaching Points

A quick review of the normal histology of ductal tissue in the breast shows a simple monolayer of epithelial cells with an underlying basement membrane.

- Despite the proliferative classification of this papilloma, the basement membrane is not violated, so there is no invasion.
- Invasion is an essential hallmark of epithelial malignancy.

Benign lesions of the breast, depending on their microscopic properties, may range in future risk of developing cancer from none at all, to a 4- to 5-fold increase.

Acknowledgment

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